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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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PENNIE & EDMONDS LLP
1155 AVENUE OF THE AMERICAS
NEW YORK, NY 10036-2711

EXAMINER

WILSON, MICHAEL C

ART UNIT PAPER NUMBER

1632

DATE MAILED: 10/27/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/369,941

Applicant(s)

KENSIL, CHARLOTTE A.

Examiner

Michael C. Wilson

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 31 July 2003 and 12 August 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 19,21-28,63-78,90,92-103 and 105-114 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 19,21-28,63-78,90,92-103 and 105-114 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 7-31-03.
- 4) ☐ Interview Summary (PTO-413) Paper No(s) _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

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DETAILED ACTION

The amendment filed 7-31-03 has been entered. Applicant's arguments filed therein have been fully considered but they are not persuasive. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 20, 80-83, 91, 104, 115 and 116 have been canceled. Claims 19, 21-28, 63-78, 90, 92-103 and 105-114 remain pending and under consideration in the instant office action as they relate to a composition comprising a) saponin and b) an immunostimulatory oligonucleotide, and to a method of using such a composition (Group II). The claims are not being examined as they relate to a composition comprising a) saponin, b) an immunostimulatory oligonucleotide, and c) an antigen, or methods of using such a composition. For examination purposes a "nucleic acid sequence encoding an antigen" is not an antigen because antigens are proteins, and because nucleic acid sequences are materially distinct and separate than proteins.

Claim Rejections - 35 USC § 112

I. Claims 19, 21-28, 63-78, 90, 92-103 and 105-114 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that

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the inventor(s), at the time the application was filed, had possession of the claimed invention.

The term "derived" (19, 63, 65, 69, 71, 73, 75, 103) does not have support on pg 5-6 as cited by applicants. While the specification contemplates obtaining saponin from *Quillaja saponaria*, the term specification does not use the term "derived," which encompasses saponin obtained from *Quillaja saponaria* as well as saponin that evolved from *Quillaja saponaria*, i.e. man-made saponin not obtained from *Quillaja saponaria*.

"Derive" has a broader meaning than "obtain."

The phrase "phosphate-modified nucleotides" does not have support in the paragraph bridging 9-10 as stated by applicants (25, 65, 66, 96, 97, 110). The citation only discusses modifying the 5' or 3' nucleotides of an oligonucleotide with phosphorothioate-modified nucleotides. Such contemplation is not equivalent to any "phosphate-modified nucleotide" as claimed.

The specification does not support administering a nucleic acid sequence encoding an antigen as newly claimed (claims 64, 67, 68, 70, 72, 74, 76, 80, 90 and 103). Pg 14, line 22, through pg 15, line 4, teach that the antigens suitable for the enhanced immune response (pg 14, line 22) may be a nucleic acid encoding the antigen (pg 15, line 1). The "immune response" on pg 14, line 22, refers to the immune response against an antigen in an individual or test system. The citation does not state the nucleic acid sequence is administered to the individual or test system or that the

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nucleic acid sequences suitable for the enhanced immune response are suitable for putting into the immune adjuvant and administering to an individual or test system. The citation merely states the immune response in the individual or test system may be against a nucleic acid sequence encoding an antigen. For example, tumor cell lines are genetically altered to artificially express antigens. The immune response in the individual or test system may be directed toward such antigens. The specification does not contemplate combining an immunostimulatory oligonucleotide, a saponin and a nucleic acid sequence encoding an antigen as newly claimed.

The phrase "wherein the nucleic acid encoding the antigen is administering to the individual or test system within 0-2 days of the administration of the immune adjuvant composition" is new matter (claim 113). Pg 18, line 9, contemplates administering saponin and an immunostimulatory oligonucleotide together or separately "within a short period of time (i.e. 0-2 days)." The specification does not contemplate administering DNA encoding an antigen and a mixture of saponin and immunostimulatory oligonucleotide together or separately. One of skill cannot extrapolate administering C and A+B together or separately as newly claimed from administering A and B together or separately as taught in the specification as originally filed. Therefore, the phrase is new matter.

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The rejection of claims 19, 21-28, 63-78, 90, 92-103 and 105-114 under 35 U.S.C. 112, first paragraph, enablement, have been withdrawn in view of the amendment to the claims.

II. Claims 19-28, 63-78, 80-83 and 90-116 are rejected and claims under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The rejection regarding the phrase "immunostimulatory oligonucleotide having an unmethylated CpG" has been withdrawn because applicants argue the phrase encompasses any nucleic acid of any length having at least one unmethylated CpG.

Claims 64, 67, 68, 70, 72, 74, 76 and 90 are unclear. The claim requires administering "an amount of the immune adjuvant of claim [] effective to induce the immune response, and wherein said individual is administered a nucleic acid... sequence encoding the antigen." The claim does not clearly set forth the steps of the claim required to induce the immune response against the antigen. Administering both the immune adjuvant and the nucleic acid sequence encoding the antigen are required to induce an immune response against the antigen; however, the claim only requires administering the immune adjuvant to induce an immune response against the antigen. The amount of "immune adjuvant" required to induce an immune response against the antigen is not defined in the specification or in the art at the time of filing.

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The phrase "inducing the immune response in an individual to an antigen" does not make sense (claims 64, 67, 68, 70, 72, 74, 76 and 90). The phrase "to an antigen" is describing the "immune response," not the "individual." In addition, it is unclear whether "the" immune response refers to one particular immune response or to any immune response against an antigen.

The metes and bounds of what applicants consider "chemically modified" saponins cannot be determined (claims 75, 77). It is unclear if the phrase encompasses any saponin isolated from *Quillaja saponaria* by chemical means or if the phrase is limited to saponins chemically modified after being isolated. It is unclear if the phrase is meant to define a purity of saponin or a structural feature of saponin.

Claims 24, 27, 28, 95, 98, 99, 108, 111 and 112 are indefinite because the limitations improperly refer back to the "motif" which no longer exists in the parent claims. Claims 24, 95 and 108, for example, would be properly further limit the parent claims written as --wherein said immunostimulatory oligonucleotide comprises more than one unmethylated CpG dinucleotide--. In claims 27, 98 and 111, replace "wherein the... ..5'X1CGX23'..." with --wherein the unmethylated CpG dinucleotide comprises 5'X1CGX23'...--. In claims 28, 78, 99 and 112, replace "wherein the CpG motif comprises" with --wherein said unmethylated CpG dinucleotide comprises--.

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Claim Rejections - 35 USC § 102

The rejection of claims 19, 24-27, 65-68, 73 and 74, 90, 95-98, 100-102, 113 and 114 under 35 U.S.C. 102(e) as being anticipated by Agrawal (US Patent 5,968,909, Oct. 19, 1999) has been withdrawn because Agrawal did not teach saponin was isolated from *Quillaja saponaria* as newly claimed and because Bomford et al. (1992) taught Saponin was isolated from sources other than *Quillaja saponaria*.

III. Claims 75, 76, 113 and 114 remain rejected under 35 U.S.C. 102(e) as being anticipated by Urban (6,013,258, Jan 11, 2000) as supported by Krieg (Trends in Microbiology, Jan. 1, 1998, Vol. 6, pages 23-26). The rejection of claims 65 and 67 has been withdrawn because Urban did not teach using phosphate-modified nucleotides.

Urban taught administering a plasmid comprising at least one unmethylated CpG dinucleotide and Quil A (col. 6, line 18). While not relied upon, the inherency of plasmid DNA having an unmethylated CpG dinucleotide is supported by Krieg who taught that plasmid DNA is bacterial DNA that has unmethylated CpG dinucleotides (pg 23, line 5; pg 25, col. 1, ¶ 1 and 2). Quil A is inherently a saponin derived from *Quillaja saponaria* and is “chemically modified” because has been removed from its natural environment by means of chemistry. The plasmid can be delivered at the same time as Quil A (col. 6, line 25), which is “within 2 days” (claim 113).

IV. Claims 75, 76, 113 and 114 remain rejected under 35 U.S.C. 102(e) as being anticipated by Sasaki (US Patent 5,808,024, Sept. 15, 1998) as supported by Krieg

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(Trends in Microbiology, Jan. 1, 1998, Vol. 6, pg 23-26) for reasons of record. The rejection of claims 65 and 67 has been withdrawn because Sasaki did not teach using phosphate-modified nucleotides.

Sasaki taught the pBluescript II SK plasmid encoding an antigen (col. 18, lines 4-19; col. 11, lines 22-45) and combining such a plasmid with QS-21 (column 3, lines 36-63; see especially lines 39 and 63). pBluescript II SK inherently has at least one unmethylated CpG dinucleotide because plasmids inherently have unmethylated CpG dinucleotides. While not relied upon, the inherency of plasmids having unmethylated CpG dinucleotides is supported by Krieg who states that plasmids are bacterial DNA that have unmethylated CpG dinucleotides (pg 23, line 5; pg 25, col. 1, ¶ 1 and 2). QS21 is inherently derived from *Quillaja saponaria* and is "chemically modified" because it has been removed from its natural environment by means of chemistry. The plasmid and saponin are administered at the same time, which is "within 2 days" (claim 113).

Claim Rejections - 35 USC § 103

V. Claims 19, 21-27, 63-68, 73-77, 90, 95-98, 100-102, 113 and 114 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Weiner (Sept. 1997, PNAS, Vol. 94, pages 10833-10837) in view of Kensil (1996, Critical Reviews in Therapeutic Drug carrier Systems, Vol. 13, No. 1 and 2, pages 1-55).

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Weiner taught administering oligonucleotide 1643 increased the humoral immune response in a mouse (page 10834, col. 1). 1643 has three unmethylated CpG motifs (pg 10834, Table 1; note the "ACGC" "TCGA" and "TCGA" = claim 27) and is phosphorothioated (pg 10833, col. 2, 11 lines from the bottom). Weiner did not teach combining 1643 with QS-7, -17, -18 or -21. However, at the time of filing, Kensil taught combining QS-7, -17, -18 or -21 with vaccines for an adjuvant effect (pg 23) and with other adjuvants to increase the adjuvant effect (pg 6, 2nd full ¶).

Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine oligonucleotide 1643 of Weiner with QS-7, -17, -18 or -21 as taught by Kensil. One of ordinary skill in the art at the time the invention was made would have recognized that 1) both Weiner and Kensil are directed toward compositions with adjuvants that increased the humoral immune response and 2) 1643 and QS-7, -17, -18 or -21 could be combined because it was common for one of ordinary skill in the art at the time of filing to combine adjuvants to increase the humoral immune response. One of ordinary skill in the art at the time the invention was made would have been motivated to combine oligonucleotide 1643 and QS-7, -17, -18 or -21 to increase the humoral immune response.

Applicants' arguments regarding the above rejection are addressed after the following rejection.

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VI. Claims 19, 21, 24, 25, 27, 28, 65, 67, 69, 70, 73-77, 90, 95-98, 100-102, 113 and 114 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Weiner (Sept. 1997, PNAS, Vol. 94, pages 10833-10837) in view of Kensil (1996, Critical Reviews in Therapeutic Drug carrier Systems, Vol. 13, No. 1 and 2, pages 1-55).

Weiner taught administering oligonucleotide 1758 increased the humoral immune response in a mouse (page 10834, col. 1) that has unmethylated CpG motifs and is equivalent to SEQ ID NO:1. 1758 is phosphorothioated (page 10833, col. 2, 11 lines from the bottom) (claims 25, 26, 55, 56 and 65-68). Weiner does not teach combining 1758 with Quil A. However, at the time of filing, Kensil taught combining Quil A with other adjuvants to increase the adjuvant effect (page 6, line and page 23). Quil A is purified from *Quillaja saponaria*, is less purified than QS-7, 17, 18 or -21 and has less of an adjuvant effect than QS-7, 17, 18 or -21 (page 3, page 5, Fig. 1, page 11).

Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine oligonucleotide 1758 of Weiner with Quil A as taught by Kensil. One of ordinary skill in the art at the time the invention was made would have recognized that 1) both Weiner and Kensil are directed toward compositions with adjuvants that increase the immune response and 2) 1758 and Quil A could be combined because it was common for one of ordinary skill in the art at the time of filing to combine adjuvants to increase the immune response. One of ordinary skill in the art

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at the time the invention was made would have been motivated to combine oligonucleotide 1758 and Quil A to increase the immune response.

Applicants argue “immunostimulatory oligonucleotides comprising at least one unmethylated CpG dinucleotide are generally expected to act in the same manner, and thus share the characteristic of synergism with saponins from *Quillaja saponaria*...” (pg 25 of response, 1st full ¶). Applicants’ argument is not persuasive. First, Weiner et al. taught oligonucleotides 1758, 1643 and 1812 induced different humoral effects (Fig. 1); therefore, different immunostimulatory oligonucleotides induce different effects. Second, some oligonucleotides having unmethylated CpG dinucleotides can be used to reduce the immune response to the oligonucleotide (Agrawal et al. of record). Third, it cannot be determined what applicants mean by such oligonucleotides sharing “the characteristic of synergism with saponins” or how such a conclusion was made. Therefore, immunostimulatory oligonucleotides having at least one CpG dinucleotides are not expected to have the same function.

Applicants argue the cellular response to oligonucleotides containing unmethylated CpG dinucleotides is mediated by a Toll-like receptor, TLR9; therefore, applicants conclude that all oligonucleotides containing unmethylated CpG dinucleotides demonstrate the same activity (pg 25 of response). Applicants’ argument is not persuasive. First, such a finding was not available to one of skill in the art at the

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time the invention was made because Hemmi et al. (2000) was published after filing the instant application. Second, the claims encompass any immune adjuvant activity and are not limited to increasing a cellular immune adjuvant activity. Third, the basis of the rejection is that both oligonucleotide 1643 and 1758 as well as QS-21 enhanced a humoral response. Finally, the fact that oligonucleotides containing unmethylated CpG dinucleotides are all processed by the TLR9 does not indicate that all bind to the same degree or that all are processed with equal efficiency and does not take into account the possibility of other structures that might improve processing of the oligonucleotides. A showing that all oligonucleotides having at least one CpG dinucleotide are processed by the same mechanism does not allow one to conclude that all such oligonucleotides have the same activity. Some are more immunogenic than others. Therefore, immunostimulatory oligonucleotides having at least one CpG dinucleotides processed by TLR9 are not expected to have the same function.

Applicants argue new oligonucleotide 2006 shows synergy in combination with QS-21. Applicants argue that it is "immaterial that oligonucleotide 2006 was not available at the time of filing, rather what is significant is that synergism was demonstrated in accordance with the teaching of the instant specification" (§ bridging pg 25-26). Applicants' arguments are not persuasive. Oligonucleotide 2006 was not taught in the specification as originally filed and, therefore, cannot be "in accordance with the teaching of the instant specification." The claims are not limited to using

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oligonucleotide 2006 and QS-21 or to oligonucleotides having an immunostimulatory activity that is distinguishable from that of the combined teachings of Weiner and Kensil. Oligonucleotide 2006 does not correlate to oligonucleotide 1643 or 1758 because they have a different structures, they induce different immune responses and because immunostimulatory oligonucleotides having at least one CpG dinucleotides are not expected to have the same function for reasons cited above.

Applicants argue the “salient feature of all three oligonucleotides is unmethylated CpG dinucleotides” (pg 26, line 6). Applicants’ argument is not persuasive. Oligonucleotides having unmethylated CpG dinucleotides can be used to reduce the immune response to the oligonucleotide (Agrawal et al. of record) or to increase a humoral response (Weiner et al.). Different oligonucleotides having unmethylated CpG dinucleotides can be used to induce different humoral immune responses (Weiner et al.). Therefore, the common feature is not merely the structural similarity of having at least one unmethylated CpG dinucleotide.

Applicants argue different “saponins isolated from *Quillaja saponaria* that possess immune adjuvant activity share a common structure, and thus would be expected to function in the same manner” (pg 26, 1st full ¶). Applicants point to Kensil of record (1993) showing the structural similarities of QS-7, -17, -18, and -21, to Soltysik of record (1995) who suggests QS-7, -17, -18, and -21 each have “a triterpene backbone and a 2, 3, glucuronic acid carboxyl group...” (¶ bridging pg 26-27) and to Liu

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of record (2002) who teaches QS-7, -17, -18, and -21 are all acetylated (pg 27, 1st ¶). Applicants' arguments are not persuasive. Kensil (1993) showed QS-7, -17, -18, and -21 were structurally different. Kensil (1991) taught QS-7, -17, -18, and -21 induced different antibody responses (pg 434, Fig. 3, Tables 1 and 2) and had different toxicities. Therefore, QS-7, -17, -18, and -21 have different structures and induce different immune responses.

Applicants have not shown that the expected immune response obtained using oligonucleotide 1643 or 1758 alone plus the expected immune response obtained using QS-21 alone is less than the immune response obtained when oligonucleotide 1643 or 1758 is combined with QS-21; this is the foundation of showing an unexpected result. The immune response of the combination must be greater than the expected additive immune response of both components alone.

VII. Claims 19, 21-27, 63-68, 71-78, 90, 95-98, 100-102, 113 and 114 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Chu (Nov. 17, 1997, J. Exp. Med., Vol. 186, pg 1623-1631) in view of Kensil (Kensil, 1996, Critical Reviews in Therapeutic Drug Carrier Systems, Vol. 13, No. 1 and 2, pg 1-55).

Chu taught administering oligonucleotide 1826 or 1760 as an adjuvant increased the IgG2a immune response in a mouse (pg 1625, col. 2, Fig. 1A and 1D). 1826 and 1760 have unmethylated CpG motifs, and 1826 is equivalent to SEQ ID NO:2. 1826

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and 1760 are phosphorothioated (page 1625, col. 1, Table 1). Chu did not teach combining 1826 or 1760 with Quil A, QS-7, -17, -18 or -21. However, Kensil taught combining Quil A, QS-7, -17, -18 or -21 with other adjuvants to increase the adjuvant effect (page 6, line and page 23). Quil A is purified from *Quillaja saponaria*, and QS-7, 17, 18 and -21 are purified from a less pure formulation of saponin. Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine oligonucleotides 1826 or 1760 of Chu with Quil A, QS-7, 17, 18 or -21 as taught by Kensil. One of ordinary skill in the art at the time the invention was made would have recognized that 1) both Chu and Kensil are directed toward compositions with adjuvants that increase the immune response and 2) 1826 or 1760 and Quil A, QS-7, 17, 18 or -21 could be combined because it was common for one of ordinary skill in the art at the time of filing to combine adjuvants to increase the immune response. One of ordinary skill in the art at the time the invention was made would have been motivated to add oligonucleotide 1826 or 1760 and Quil A, QS-7, 17, 18 or -21 to increase the IgG2a immune response.

Applicants' arguments are addressed above. In addition, Chu taught 1826 and 1760 as well as other oligonucleotides sharing similar structures (i.e. at least one unmethylated dinucleotide) induced different immune responses (Fig. 1-5).

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The limitation of a CpG motif having the formula 5' X_1 CG X_2 3' in claim 27, 98 and 111 still cannot be searched because the nucleic acid is so small and may be part of any plasmid, which is very large in comparison, and cannot be adequately searched on computer databases or by eye.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

No claim is allowed.

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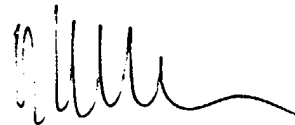
Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Wilson who can normally be reached on Monday through Friday from 9:00 am to 5:30 pm at (703) 305-0120.

Questions of a general nature relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-1235.

If attempts to reach the examiner, patent analyst or Group receptionist are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached on (703) 305-4051.

The official fax number for this Group is (703) 872-9306.

Michael C. Wilson

A handwritten signature in black ink, appearing to read 'Michael C. Wilson', with a stylized, flowing script.

MICHAEL WILSON
PRIMARY EXAMINER